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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/069,062 | 02/21/2002 | John David Charles Rosamund | 056291-5073 | 8999 |

9629 7590 10/21/2003

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WASHINGTON, DC 20004

| EXAMINER | |
|---|---|
| BASKAR, PADMAVATHI | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1645 | 9 |

DATE MAILED: 10/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/069,062 | ROSAMUND ET AL. | |
| | Examiner | Art Unit | |
| | Padmavathi v Baskar | 1645 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *8/1.03* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,2,10 and 15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,10 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: Notice to Comply Sequence rules.

## DETAILED ACTION

1. Applicant's response to restriction requirement filed on 8/1/03 is acknowledged. Applicant states that claims 2-9 and 11-14 have been cancelled. However, it is noted that claim 2 is not cancelled since claim has been amended and is drawn to the elected group I. Therefore, Claims 3-9 and 11-14 have been canceled. Claims 1, 2, 10 and 15 are pending and are under examination.

### Priority

2. This application is a national stage entry of PCT/GB00/03100 International Filing Date: 08/15/2000, which claims priority to

| | | |
|---|---|---|
| 9919766.7 | 08/21/1999 | UNITED KINGDOM |

The examiner has reviewed the priority document and found support for claims 1, 2, 10 and 15 with respect to SEQ.ID.NO: 7. Therefore, the priority is accorded as of the filing date 08/21/1999 of U.K. 9919766.7.

### Specification - Informalities

3. This application has not followed the directions or order or arrangement in framing the specification as mentioned above. There is no brief description of the drawing as set forth in 37 C.F.R.1.74.

### Sequence Requirements

4. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. 1.821-1.825 for the reason(s) set forth below:

The specification on page 17 discloses four oligonucleotide sequences, identified by Sequence identification Numbers, SEQ.ID.NO: 12, 13, 14 and 15. However, these sequences are not disclosed and are not in compliance with the sequence rules.

5. Full compliance with the sequence rules is required in response to this office action.

**Drawings**

6. The drawings are accepted by the draftsperson under 37 C.F.R. 1.84 or 1.152.

**Election**

7. Applicant's election of Group I claim 1, 2, 10 and 15 drawn to the polypeptide SEQ.ID.NO: 7 in Paper # 8 filed on 8/1/03 is acknowledged. Applicant is advised to amend the claim 15 with respect to the elected invention (i.e., polypeptide).

**Claim Rejections - 35 USC 112**

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1, 2, 10 and 15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The instant specification does not disclose (1) a sequence possessing at least 80% similarity, (2) isolated polypeptide of at least 15 contiguous amino acids of the polypeptide of

claim 1, (3) a method to identify compounds that inhibit phosphomevalonate kinase (PMK) activity comprising contacting test compound with said sequence possessing at least 80% similarity or an isolated polypeptide of at least 15 contiguous amino acids of the polypeptide and (4) a diagnostic kit for detecting the presence of C.albicans comprising antibodies capable of binding to a sequence possessing at least 80% similarity or an isolated polypeptide of at least 15 contiguous amino acids of the polypeptide in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing.

The specification discloses an isolated polynucleotide sequence, phosphomevalonate kinase (PMK) that is described as ERG 8 gene from C.albicans and its encoding polypeptide, SEQ ID NO: 7. Applicants also broadly describe the invention as embracing any substitution, insertion or deletion change of nucleotides throughout the entire stretch of nucleotides found in the encoding sequence by use of language in which a specified polypeptide sequence which is at least 80% identical to the polypeptide sequence of SEQ.ID.NO 7, (2) isolated polypeptide of at least 15 contiguous amino acids of the polypeptide of claim 1, (3) a method to identify compounds that inhibit phosphomevalonate kinase (PMK) activity comprising contacting test compound with said sequence possessing at least 80% similarity or an isolated polypeptide of at least 15 contiguous amino acids of the polypeptide and (4) a diagnostic kit for detecting the presence of C.albicans comprising antibodies capable of binding to a sequence possessing at least 80% similarity or an isolated polypeptide of at least 15 contiguous amino acids of the polypeptide. None of these sequences and the method using these sequences meets the written description provision of 35 U.S.C. 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The

invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she] invented what is claimed." (See Vas-Cath at page 1116.). One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

10. Claims 1, 2, 10 and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated and purified polypeptide comprising the amino acid sequence, SEQ. ID. NO: 7, a method to identify compounds that inhibit PMK activity of C.albicans, said method comprising contacting the test compound and the polypeptide SEQ.ID.NO: 7 and a diagnostic kit for detecting C.albicans comprising antibodies binding to the polypeptide SEQ.ID.NO: 7 does not reasonably provide enablement for (1) a sequence possessing at least 80% similarity, (2) isolated polypeptide of at least 15 contiguous amino acids of the polypeptide of claim 1, (3) a method to identify compounds that inhibit phosphomevalonate kinase (PMK) activity comprising contacting test compound with said sequence possessing at least 80% similarity or an isolated polypeptide of at least 15 contiguous amino acids of the polypeptide and (4) a diagnostic kit for detecting the presence of C.albicans comprising antibodies capable of binding to a sequence possessing at least 80% similarity or an isolated polypeptide of at least 15 contiguous amino acids of the polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification discloses an isolated polynucleotide sequence, phosphomevalonate kinase (PMK) that is described as ERG 8 gene from C.albicans and its encoding polypeptide, SEQ ID NO: 7. However, it fails to disclose a sequence possessing at least 80% similarity to

SEQ.ID.NO: 7, isolated polypeptide of at least 15 contiguous amino acids, a method to identify compounds that inhibit phosphomevalonate kinase (PMK) activity comprising contacting test compound with said sequence possessing at least 80% similarity or an isolated polypeptide of at least 15 contiguous amino acids of the polypeptide and a diagnostic kit for detecting the presence of C.albicans comprising antibodies capable of binding to a sequence possessing at least 80% similarity or an isolated polypeptide of at least 15 contiguous amino acids of the polypeptide . Examiner has reviewed the specification and found no support for such language. The specification recites polypeptide SEQ.ID.NO 7. However, there is no support for a fragment with 80% similarity or fragments of at least 15 contiguous amino acids or method or kit using said fragments. Therefore, applicant is advised to point to the specification where support for this claimed language is drawn and how it conveys the concept of the instant claims.

Scope of enablement requires that the specification teach those in the art to make and use the invention commensurate with the scope of the claim without undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The instant claims comprising fragments with 80% similarity or fragments of 15 amino are not predicted. The specification provides guidance and direction with regard to SEQ.ID.NO However, there is no guidance or directions on how to make and how to use a polypeptide comprising fragments or variants of SEQ.ID.NO: 7. It is known in the art that deletions, or modifications of the amino acids of a protein alter the function of the protein. The amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and still retain similar activity/utility

requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, the problem of predicting protein structure from mere sequence data of a single protein and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex (Bowie et al. Science, Vol. 247: 1990; p. 1306; p. 1308) and is well outside the realm of routine experimentation.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple modifications of other types and the positions within the protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining similar activity/utility are limited in protein and the result of such modifications is unpredictable based on the instant disclosure.

The specification does not support the broad scope of the claims which encompass a nucleic acid molecule encodes a fragment which can be predictably modified and which regions are critical; what variants, if any, can be made which retain the biological activity of the intact protein; and the specification provide essentially no guidance as to which of the essentially infinite possible choices is likely to be successful. Further, Houghten et al. (Vaccines, 1986, Edited by Fred Brown: Cold Spring Harbor Laboratory) teach that changes/modifications (addition, substitution, deletion or inversion) of one or more amino acids in a polypeptide will alter antigenic determinants and therefore affect antibody production (p. 21) as well as antibody binding. Houghten et al. also teach that "... combined effects of multiple changes in an antigenic determinant could result in a loss of [immunological] protection." And "a protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations at key

residues could create a new antigen that is precipitously or progressively unrecognizable by any of the antibodies..." (p. 24). Houghten et al. teach that point mutations at one key antigen residue could eliminate the ability of an antibody to recognize this altered antigen (p. 24). It is not always possible to make the derivatives that retain immunodominant regions and immunological activity if the regions have been altered. The specification teaches that specific primer or probes are required to amplify the PMK gene that encodes the polypeptide or its use in diagnostic for C.albicans. Therefore, any fragment or variant would not work in diagnostic kit for C.albicans or a method to identify compounds that inhibit PMK activity of the polypeptide.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed polypeptide i.e., fragment with 80% similarity or fragments of 15 contiguous amino acids in a method or in a diagnostic kit in a manner reasonably correlated with the scope of the claims broadly including any as presently claimed. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made in the protein renders activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. The sequence of some proteins is highly conserved and one skilled in the art would not expect tolerance to any amino acids modification in such proteins. However, even if it were shown that some modifications could be tolerated in the claimed peptide, for the reasons discussed the claims would still expectedly encompass significant changes; which could not be distinguished without undue experimentation. See Amgen, Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991) at 18 USPQ2d 1026-1027 and Ex parte Forman, 230 U.S.P.Q. 546 (Bd. Pat. App. & Int. 1986).

***Status of Claims***

11. No claims are allowed.

***Conclusion***

12. SEQ.ID.NO: 7 is free of prior art

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padma Baskar whose telephone number is (703) 308-8886. The examiner can normally be reached on Monday through Friday from 6:30 AM to 4 PM EST

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Padma Baskar Ph.D.

10/20/03

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

## NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: The specification on page 17 discloses four oligonucleotide sequences, identified by Sequence identification Numbers, SEQ.ID.NO: 12, 13, 14 and 15. However, these sequences are not disclosed and are not in compliance with the sequence rules.

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### Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirement ease contact:

For Rules Interpretation, call (703) 308-4216
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